

Virtual Enlightenment Salon

FDA Reform Panel Preliminary Presentation

April 4th, 2021

Dr. Dan Elton



Setting the stage...

- Since 1962, to bring a drug to market companies must not only prove **safety** but also **efficacy**, using large randomized controlled trials (RCTs).
- The trials are very **expensive** relative to observational trials and take 1-6 years to complete.
- It takes another **6 – 18 months** for the FDA to review the trial results.
- FDA uses excess **precaution**. Sometimes they require another phase III.
- Many companies can't swallow the high costs (**\$10 - \$100 million per trial**)
- Companies stick to variants of what is known – too expensive and risky to invest in in new molecules and modalities where failure rate may be high.

A glaring inconsistency:

Many very risky and/or harmful substances are legal:

Tobacco

Vapes

Alcohol

Marijuana

Possession of hard drugs (in some states)

Big Gulp sodas

But doctors cannot prescribe potentially helpful drugs that have passed safety tests and may have science behind them (ie animal models / biomarker studies) ...

... instead, they must wait 1 - 6 years

... Some useful treatments are
never approved..

The invisible graveyard

- Media will report a lot when an FDA drug has unexpected side effects (Vioxx scandal, etc etc)
- Deaths and suffering from delays and non-approval of useful drugs (type II errors) don't get any attention.
- Economists and other researchers estimate the numbers are huge – 100,000+ deaths per year (see work by Dr. Mary J. Ruwart)



The Invisible Graveyard is Invisible No More

by [Alex Tabarrok](#) January 29, 2021 at 7:25 am in **Economics, Law, Medicine**

- For months, US Taxpayers have been desperate for the vaccines they paid for.
 - Long lines, people traveling hundreds of miles
 - Thousands dying every day
 - Many more suffering from social isolation, loss of loved ones, & job loss
- People are frustrated and starting to ask questions.
- Why was Pfizer's vaccine EUA pushed from early November to late December?
- Why 30 million doses of AstraZeneca's vaccine in warehouses that can't be used?



Very fast rundown of some FDA reform ideas

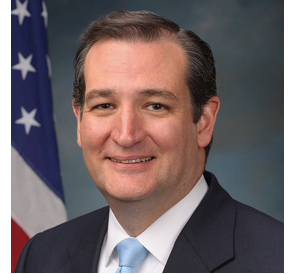
Reform idea #1 Improving transparency

- Key decisions are made behind closed doors
- Congress should mandate a structured report with a cost benefit analysis on every decision to be published before the decision goes into effect

Reform idea #2 Reciprocity

- If a drug/medication is approved by a regulatory agency in a different country which has equivalent standards to the FDA (ie UK, japan, EMA...), it should automatically be approved by the FDA

Reciprocity Ensures
Streamlined Use of
Lifesaving Treatments
(**RESULT**) **Act**



Reform idea #3

Making the agency independent from the executive branch

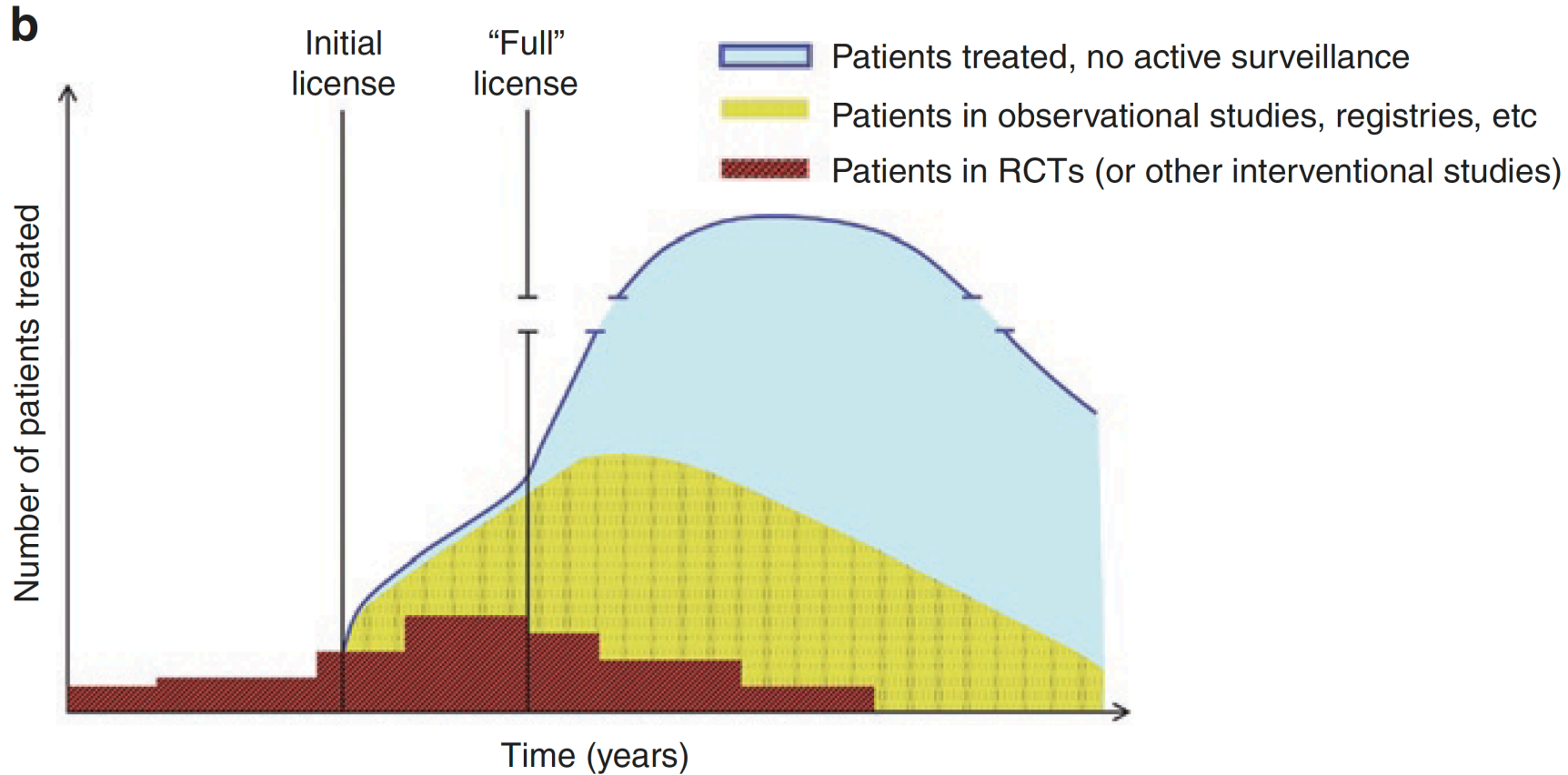
- Free agency from political meddling from HHS and the President
- Has a lot of support within FDA



Reform idea #4 Rolling reviews

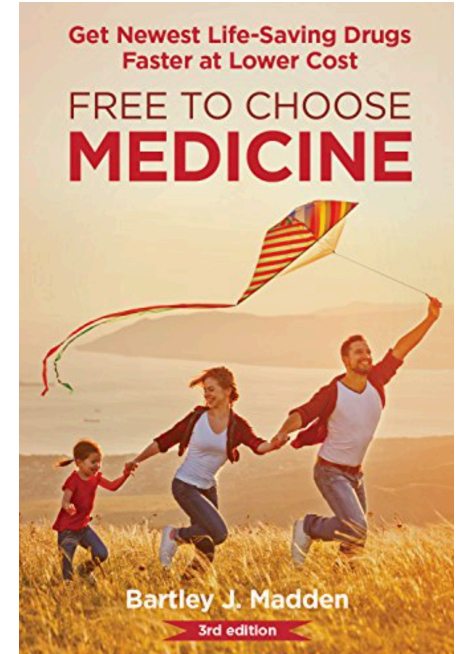
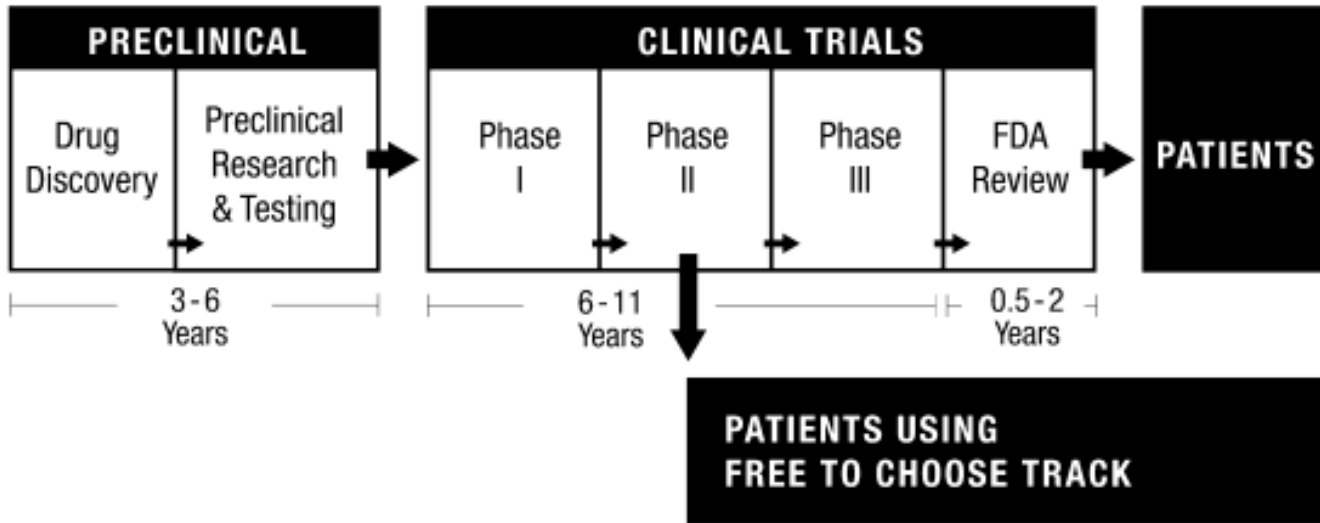
- EUAs should not take 4 weeks
- Approvals should not take 6 – 18 months

Reform idea #5 : Adaptive licensing



Eichler et al. *Clinical Pharmacology & Therapeutics*, **91**: 426-437.

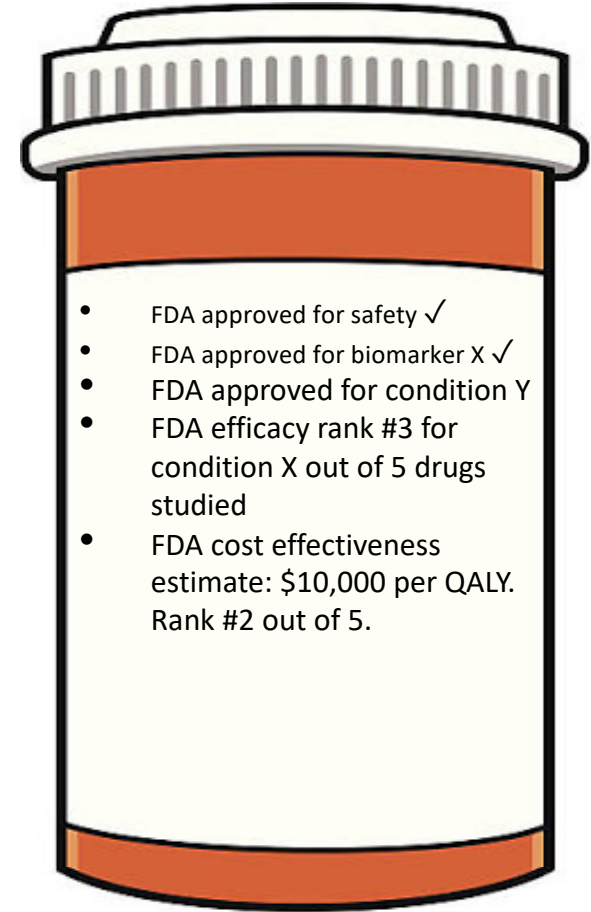
Reform idea #6 : Free to choose medicine



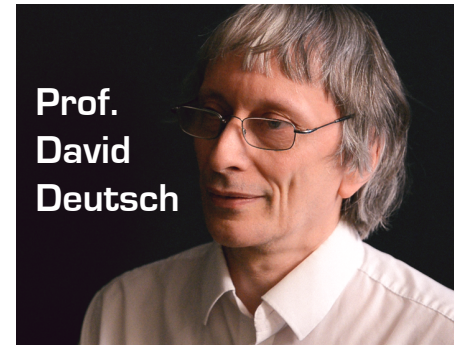
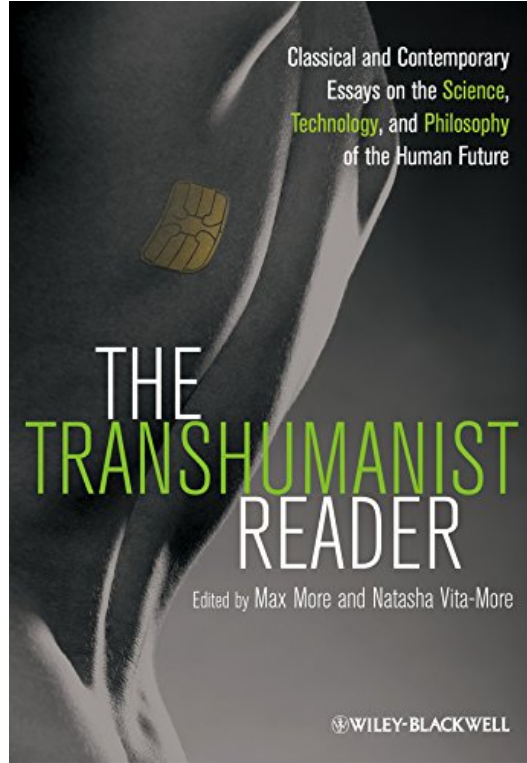
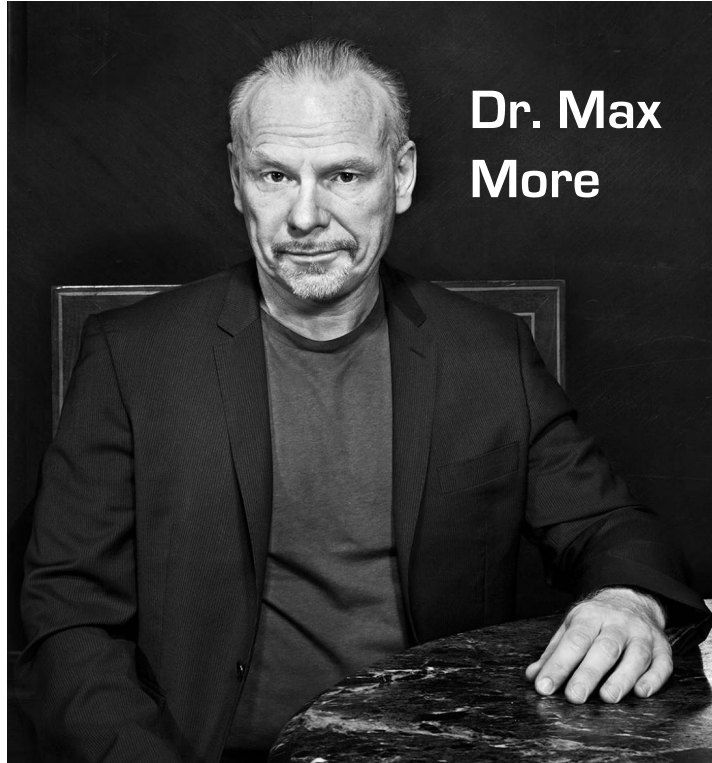
Reform idea #7 – Tiered approval, etc



Nutrition Facts	
Serving size	4 oz (113g)
Amount per serving	
Calories	240
% Daily Value*	
Total Fat 14g	18%
Saturated Fat 8g	40%
Trans Fat 0g	
Cholesterol 0mg	0%
Sodium 370mg	16%
Total Carbohydrate 9g	3%
Dietary Fiber 3g	11%
Total Sugars <1g	
Includes <1g Added Sugars	1%
Protein 19g	31%
Vitamin D 0mcg	0%
Calcium 170mg	15%
Iron 4.2mg	25%
Potassium 610mg	15%
Thiamin	2350%
Riboflavin	15%
Niacin	50%
Vitamin B ₆	20%
Folate	30%
Vitamin B ₁₂	130%
Phosphorus	15%
Zinc	50%
*The % Daily Value tells you how much a nutrient in a serving of food contributes to a daily diet. 2,000 calories a day is used for general nutrition advice.	



Reform idea #8 : the Proactionary Principle as a foundation for rational structured cost-benefit analysis at the FDA



The precautionary principle:

“When an activity raises threats of harm to human health or the environment, precautionary measures should be taken even if some cause and effect relationships are not fully established scientifically.”

1998 Wingspread Statemetn

The precautionary principle....

- Is **irrational** - asymmetrical focus on cost/benefit of action, ignores inaction
- Is **vague** – subject to human biases
- Is **anti-progress** - All progress requires risk as an input. (cf David Deutsch)
- Is **pessimistic** – humans can't deal with risk
- Is **ultraconservative** – protects the status quo and existing institutions and power structures from change
- Is **wasteful** – excessive time & money are spent on risk minimization
- Is **anti-technology and pro-nature** – focus only on man-made risks while ignoring risks from nature. (naturalistic fallacy)

The proactionary principle...

- Is **rational** – symmetrical treatment of cost/benefit of action *and* inaction
- Is **specific** – maximize diversity of values (not just safety) using quantitative cost-benefit analysis
- Is **pro-progress** - All progress requires risk as an input. (cf David Deutsch)
- Is **optimistic** – humans *can* deal with risk if we tackle it with structured, careful decision making
- Is **progressive** – *rejects* the status quo - it's not good enough!
- Is **efficient** – time and money are focused where they can do the most good
- Is **neutral to both technology and nature** – the costs and benefits of both are given equal consideration, neither is biased over the other.

“Underlying More’s whole discussion is a deep appreciation for the great economic concept of **opportunity cost**. The progress you don’t see because you didn’t allow change is as much a cost as the losses you do see because you did. It’s only because some places and times allowed drastic change that we can look back in time to 1000 A.D... and realize how lucky we are that proaction prevailed over precaution.”

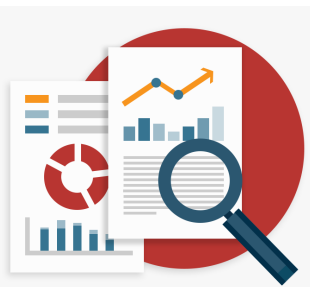
-- Prof. Bryan Caplan

The Proactionary Principle

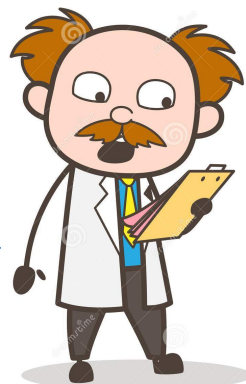


Developing a balanced approach to decision making

Two paths for FDA reform



Strong case for reform based on **rigorous quantitative analysis** that is grounded in good epistemology and ethics.



Distilled talking points



Path 1: meet with patients and patient advocacy groups. Lots of TEDx type talk(s) and op-eds



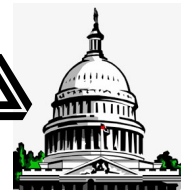
Critical mass of angry voters

Politicians make policy changes under pressure from voters



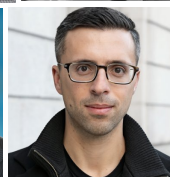
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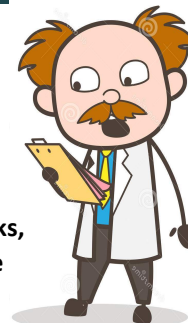


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THE HENRY J. KAISER FAMILY FOUNDATION



Path 2: meetings with key DC "influencers", think tank policy wonks, and congressional staffers from both sides of the red-blue divide



DC insiders convince politicians to make changes, get them "slipped in" a bill w/o most voters even knowing

Final thoughts....

Many exciting technologies are being developed today

- Artificial intelligence
- Genomic medicine
- Stem cell therapies
- Anti-aging / rejuvenation biotech
- Gene therapies
- mRNA vaccines

Government should make big investments in regulatory science

- Universities should teach courses on regulatory science
- Gov should hire technologists and pay them high salaries at FDA
- Test FDA decision makers and leaders for tech knowledge and send those who don't pass to early retirement
- Gov should increase funding in clinical trials
- Gov economists should calculate “value of information” of potential trials

This has nothing to do with libertarianism! It is about saving lives!

Thanks for listening!

The FDA is not equipped for the personalized genomic medicine revolution



Figure from:

Schork, N. J., “Personalized Medicine: Time for One-Person Trials.” *Nature*, 2015. **520**(7549): pp. 609–611.

THE DIGITAL FUTURE OF MOLECULAR MEDICINE: Rethinking FDA Regulation

Peter Huber
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